



Original Article

Early postoperative recurrences for colon cancer: Results from a Pakistani rural cohort

Shah Zeb Khan, MD^{a,*} and Ismat Fatima, PhD^b

^a Department of Clinical Oncology, Bannu Institute of Nuclear Medicine Oncology and Radiotherapy (BINOR), Bannu, Pakistan

^b Department of Clinical Research, Institute of Nuclear Medicine Oncology, Lahore, Pakistan

Received 2 January 2020; revised 2 March 2020; accepted 4 March 2020; Available online 3 April 2020



المخلص

أهداف البحث: أجريت هذه الدراسة لتحديد العوامل المرتبطة برجوع الورم المبكر بعد الجراحة لمرضى سرطان القولون والمستقيم الذين عولجوا بهدف الشفاء.

طرق البحث: تم مراجعة جميع المرضى على التوالي الذين خضعوا للاستئصال العلاجي لسرطان القولون والمستقيم في الفترة من يناير ٢٠١٤ إلى ديسمبر ٢٠١٦. تلقى جميع المرضى إما العلاج الكيميائي المساعد أو تمت متابعتهم في معهد بانو لطب الأورام والعلاج الإشعاعي. ينتمي المرضى إلى المناطق الريفية في جنوب مقاطعة خيبر بختونخوا.

النتائج: سجلنا ٧٢ مريضاً؛ ٢٨ منهم لديه رجوع للورم بعد الجراحة في خلال السنتين الأولى (رجوع مبكر). في تحليل أحادي المتغير، وكان الانتكاس المبكر لمرضى سرطان القولون مرتبطاً بشكل ملحوظ بالتقدم في السن أكثر من ٦٠ عاماً. الحالة العقدية، المرحلة المرضية، عدد العقد التي استوصلت والانتشار حول الشرج. باستخدام التحليل المتعدد المتغيرات، كان تجاوز العمر ٦٠ عاماً واستئصال أقل من ١٢ عقدة ليمفاوية تنبؤات مستقلة للرجوع المبكر للورم. سجل الكبد الموقع الأكثر شيوعاً للانتشار (٤٢.٨٪) في هذه الدراسة.

الاستنتاجات: أظهرت الدراسة أن السن المتقدم واستئصال أقل من ١٢ من العقد الليمفاوية أثناء الجراحة هي تنبؤات كبيرة للرجوع المبكر بعد الجراحة. تحديد هؤلاء المرضى ذوي المخاطر العالية أثناء المتابعة بطرق علاجية مطورة يمكن أن يحسن البقاء على قيد الحياة بدون مرض.

الكلمات المفتاحية: سرطان القولون؛ الظهور المبكر؛ بعد العملية؛ التنبؤات؛ البقاء على قيد الحياة بدون مرض

Abstract

Objectives: We conducted this study to determine the factors associated with early postoperative recurrence in colon cancer patients treated with curative intent.

Methods: All consecutive patients who underwent curative resection for colon cancer between January 2014 and December 2016 were reviewed. All patients received either adjuvant chemotherapy or follow-up at the Bannu Institute of Nuclear Medicine Oncology and Radiotherapy (BINOR). The patients lived in rural areas of southern Khyber Pakhtunkhwa province.

Results: We enrolled 72 patients, 28 of whom experienced a postoperative recurrence within 2 years (early recurrence). In univariate analysis, postoperative early relapse was significantly correlated with advanced age (>60 years, $p = 0.030$), nodal status ($p = 0.012$), pathological stage ($p = 0.013$), number of nodes removed ($p < 0.001$), and perineural invasion ($p = 0.044$). In multivariate analysis, age more than 60 years ($p = 0.031$) and fewer than 12 lymph nodes removed ($p = 0.003$) were independent predictors for early recurrence. The liver was the most common site of recurrence (42.8%) in this study.

Conclusion: Our results showed that advanced age and the removal of fewer than 12 lymph nodes during surgery were significant predictors for early postoperative recurrence. Identification of high-risk patients during follow-up with enhanced therapeutic modalities can improve disease-free survival.

* Corresponding address: Department of Clinical Oncology, Bannu Institute of Nuclear Medicine Oncology and Radiotherapy (BINOR), Bannu, Khyber Pakhtunkhwa, 28100, Pakistan.

E-mail: skhanizhere0@gmail.com (S.Z. Khan)

Peer review under responsibility of Taibah University.



Keywords: Colon cancer; Disease-free survival; Early recurrence; Postoperative; Predictors

© 2020 The Authors.

Production and hosting by Elsevier Ltd on behalf of Taibah University. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Colorectal cancer (CRC) is the second leading cause of mortality among all cancers worldwide.¹ The incidence and mortality of colorectal cancer varies globally mostly by race and ethnicity, with recent data suggesting the highest number of deaths due to CRC in blacks.² In the US, CRC is the second leading cause of cancer-related deaths.³ In the Eastern Mediterranean Region (EMR), there has been an increase in CRC mostly among populations aged less than 50 years.⁴ The incidences of CRC are relatively lower in Arab countries than worldwide but the population is much younger than reported previously.⁵

Pakistan has no national cancer registry; thus, incidence and mortality data are lacking. Previous single-institution studies in Pakistan indicated that colon cancer is mostly seen in younger populations.⁶ An annual report from Shaukat Khanum Memorial Cancer Hospital, Lahore reported CRC to be the second most common malignancy diagnosed among patients in 2016.⁷

The number of CRC cases is increasing, especially in low- and middle-income countries. The adoption of western lifestyles and lack of screening programmes may have contributed to the increased colon cancer incidence. The environmental risk factors linked to CRC are alcohol, tobacco use, obesity, excessive fat use, and red meat intake.⁸ Colon cancer can be either sporadic or familial. The two most common inherited forms of CRC are hereditary non-polyposis colorectal cancer (HNPCC) and familial adenomatous polyposis (FAP).

Standard colectomy with regional lymphadenectomy is performed for colon cancer patients treated with curative intent. Three to six months of perioperative chemotherapy is the standard of care for high-risk stage II and stage III disease. The overall 5-year survival rate is 60–65%, with recurrence rates varying from 30 to 40% in patients treated with curative intent. Almost 60–80% of recurrences occur within 2 years after successful treatment. Postoperative recurrence is associated with cancer-related death in most cases. In stage IV colorectal cancer, a subset of cases with liver metastasis can be treated with curative intent. Recent advancements in molecular profiling and novel agents such as bevacizumab and cetuximab or panitumumab have improved the survival of stage IV CRC.

Several prognostic factors adversely affecting disease outcomes have been evaluated in recent decades, including male sex, advanced stage, high grade, mucinous histology,

lymphovascular invasion (LVSI), perineural invasion (PNI), and high serum carcinoembryonic antigen (CEA) levels.^{9,10}

More than 60% of the population in Pakistan resides in rural areas, which lack specialized health units. Bannu Institute of Nuclear Medicine Oncology and Radiotherapy (BINOR) was established in 2012 to provide standard clinical oncology care to the population of southern Khyber Pakhtunkhwa (KPK). Standard histopathology and surgical oncology departments are also lacking in this region. Most of the population is uneducated and has financial constraints. In this context, we aimed to identify the prognostic factors predicting early recurrence after curative surgery in our rural population.

Materials and Methods

We retrospectively reviewed colon cancer patients treated with curative intent between January 2014 and December 2016 for which a complete pathological report was available, inclusive of clinicopathological characterizations. Manual patient records were obtained from the hospital cancer registry. The patients resided in rural areas of District Bannu, Karak, Lakki Marwat, Dera Ismail Khan, Tank, Kohat, and Waziristan Agency. All included patients were aged 18 years or above.

The patients underwent standard colectomy with or without regional lymphadenectomy at Tertiary Care Hospitals of Khyber Pakhtunkhwa Province. All patients received adjuvant chemotherapy for high-risk stage II and stage III colon cancer for 6 months postoperatively. Four chemotherapy regimens were used; namely, modified 5-fluorouracil, leucovorin, and oxaliplatin (mFOLFOX-6), capecitabine and oxaliplatin (CapOx), infused 5-fluorouracil/leucovorin (5FU/LV), and bolus 5FU/LV. The doses were calculated according to the patients' body surface area (BSA).

We included both locoregional and distant recurrences in our estimation of disease-free events within 2 years of successful treatment completion. Recurrences were confirmed radiologically by computed tomography (CT) or positron emission tomography-CT (PET-CT) or by surgical intervention with histopathology. Early postoperative recurrence was defined as recurrence within 2 years after surgery.¹¹

The follow-up protocol followed in BINOR included a colonoscopy 1 year after surgery, with yearly chest X-ray and CT of the abdomen and pelvis up to 5 years.

The clinic-pathological variables included for analysis were laterality, tumour size, tumour stage, nodal stage, anatomical stage grouping, number of nodes removed, LVSI, PNI, grade, and histological type.

Statistical methods

Data were analysed using IBM SPSS Statistics for Windows, version 20.0. The univariate analysis of clinic-pathologic features between the two groups was compared using chi-square tests. Independent predictive factors for postoperative early recurrence were determined by

multivariate Cox proportional hazards regression analysis. P-values <0.05 were considered statistically significant.

Results

Patient characteristics

This study included 45 men and 27 women with a median age of 52.5 years. Right and left-sided colon cancer occurred in 38 and 34 patients, respectively. The median tumour size

Table 1: Univariate analysis of the correlations between postoperative early recurrence and the clinicopathologic features of patients with resected colon cancer.

Variable	No Recurrence (n = 44)	Early Recurrence (n = 28)	P-value
Age (years) ≤60/>60	39 (88.6)/5 (11.4)	19 (67.9)/9 (32.1)	0.030
Sex: Male/Female	29 (65.9)/15 (34.1)	16 (57.1)/12 (42.9)	0.454
Laterality: Right/Left	23 (52.3)/21 (47.7)	15 (53.6)/13 (46.4)	0.914
T stage: pT3/pT4	19 (43.2)/25 (56.8)	15 (53.6)/13 (46.4)	0.389
T size (cm): <5/>5	20 (45.5)/24 (54.5)	16 (44.4)/12 (33.3)	0.334
N stage: pN0+ or pN1+ or NA/pN2	38 (89.4)/6 (13.6)	17 (60.7)/11 (39.3)	0.012
Pathological stage TNM: Stage II/III/NA	17 (38.6)/26 (59.1)/1 (2.3)	2 (7.1)/25 (89.3)/1 (3.6)	0.013
Nodes removed (number): <12/>12	17 (38.6)/27 (61.4)	25 (89.3)/3 (10.7)	<0.001
Resection margins: Positive/Negative/NA	0 (0)/44 (100)/0 (0)	2 (7.1)/25 (89.3)/1 (3.6)	0.085
LVI: Yes/No/NA	18 (40.9)/21 (47.7)/5 (11.4)	13 (46.4)/10 (35.7)/5 (17.9)	0.545
PNI: Yes/No/NA	13 (29.5)/16 (36.4)/15 (34.1)	2 (7.1)/10 (35.7)/16 (57.1)	0.044
Grade: 2/3/NA	42 (95.5)/2 (4.5)/0 (0)	22 (78.6)/4 (14.3)/2 (7.1)	0.060
Histology: Mucinous/Signet ring cells/ Adenocarcinoma not otherwise specified	9 (20.5)/4 (9.1)/31 (70.5)	7 (25.0)/6 (21.4)/15 (53.6)	0.247

Table 2: Correlations between postoperative early recurrence and clinic-pathologic features of resected colon cancer patients by multivariate Cox proportional hazards regression analysis.

Variables	Coefficient	SE	P-value	Odds Ratio	95% CI
Age ≤60 vs. >60 years	-2.323	1.079	0.031	0.098	0.012–0.812
Nodes removed ≤12 vs > 12	3.123	1.039	0.003	22.713	2.963–174.081

Table 3: Sites of recurrence in 28 patients with early postoperative recurrence.

Recurrence site	Frequency (%)
Liver	12 (42.86)
Lung	8 (28.57)
Locoregional	2 (7.14)
Multiple sites	6 (21.43)

was 4.2 cm and 36 patients had a tumour size >5 cm. Fifty-one patients were diagnosed with stage III disease and 17 patients with pathological N2 disease. Forty-two patients underwent inadequate lymph node dissection during surgery, with fewer than 12 nodes removed. Only two patients had positive margins in examination of histopathological specimens after surgery. Moderately differentiated tumours were observed in 64 patients and 31 patients were positive for LVSI. 15 patients had PNI. Tumour histology included adenocarcinoma not otherwise specified (NOS) and mucinous adenocarcinoma in 36 and 16 patients, respectively. The details of the clinic-pathological features are shown in [Table 1](#).

Postoperative early recurrence

In this study, 28 patients (38.9%) experienced a recurrence within 2 years after curative surgery. Univariate analysis revealed that age ($p = 0.030$), nodal status ($p = 0.012$), stage ($p = 0.013$), number of nodes removed ($p < 0.001$), and PNI ($p = 0.044$) were significantly correlated with postoperative early recurrences ([Table 1](#)). A multivariate cox proportional hazard analysis performed to ascertain the effect of age, stage, number of lymph nodes present, number of lymph nodes dissected, and perineural invasion on the likelihood of recurrence showed that age and number of lymph nodes dissected were significant contributors to early recurrence ([Table 2](#)).

Patients with fewer than 12 lymph nodes removed had a 22.7-fold increased risk of recurrence as compared to the risk in patients with more than 10 lymph nodes removed (HR = 22.71, 95% CI = 2.963–174.081, $p = 0.003$). In contrast, patients aged ≤60 years had a 0.098-fold lower risk of recurrence as compared to the risk in patients aged >60 years (HR = 0.098, 95% CI = 0.012–0.812, $p = 0.031$). The liver was the most common site of recurrence (42.86%), followed by the lungs (28.57%) ([Table 3](#)).

Discussion

In our study, 28 (38.9%) patients had early postoperative recurrences. The recurrence rates within 2–3 years of curative resection in previous studies were approximately 65–80% depending upon stage and other prognostic factors.^{9,12} The prognostic factors for recurrence identified by multivariate analysis in our study were age and number of nodes removed during surgery.

Early recurrence in colon cancer is a major clinical problem worldwide despite the use of adjuvant therapies. There is an urgent need to identify the prognostic factors associated with recurrence to identify high-risk populations. In Pakistan, data on treatment outcomes and survival are generally lacking. Univariate analysis in the present study showed nodal status, advanced stage, and perineural invasion to be predictive for early postoperative recurrence. Three Japanese clinical trials on colon cancer showed that lymph node metastasis and advanced stage increased the risk of recurrence within 3 years after curative resection.¹³ Another study showed advanced T and N stages were associated with increased risks of recurrence in both univariate and multivariate analyses.¹⁴ In a retrospective analysis, Elferink et al. reported increased risks of locoregional recurrence for T3-T4 and node-positive tumours.¹⁵ Early recurrences were also reportedly more common in male patients with advanced T and N stages at presentation, PNI, and lack of adjuvant chemotherapy in stage III disease.¹⁶

In the present study, multivariate analysis showed that age >60 years and the retrieval of fewer than 12 lymph nodes during surgery were predictors for early recurrence. A previous study reported that young age was associated with more recurrences but observed poor survival in patients more than 80 years of age.¹⁷ These results are contrary to those in our study; however, in our study, more than 80% of patients were <60 years of age, which may have affected our results. Older populations could be at an increased risk for recurrence in our populations; other explanations include suboptimal chemotherapy doses as well as substandard surgeries and treatment gaps, as seen in our rural population. However, one study showed an increased risk of late recurrence with advancing age.¹⁸ As our study only analysed early recurrence, studies with longer follow-up are warranted.

In our study, the resection of fewer than 12 lymph nodes during surgery was associated with a significant, approximately 23-fold increased risk of early recurrence compared to that in patients with resection of more than 10 nodes. The intergroup trial 0089 analysis showed that retrieval of more than 15 nodes positively affected overall survival (OS) and disease-free survival (DFS)¹⁹ and suggested this value should be used as a prognostic factor in future trials. Previous studies also showed that advanced stage and dissection of fewer than 12 lymph nodes were associated with poor outcome in regards to DFS.²⁰ One study showed that a cut-off of at least 20 lymph nodes during surgery was more appropriate to establish colon cancer prognosis.²¹ A study on stage II colon cancer reported that T4 tumours and dissection of fewer than 12 lymph nodes were independent risk factors for colon cancer recurrences.²² As the literature

suggests, the number of lymph nodes removed during surgery has prognostic implications, especially on event-free survival. The lack of surgical oncology units and low uptake of multidisciplinary discussions in our region have contributed to suboptimal surgeries. Histopathology reports often lack information about predictive markers for prognosis such as LVSI and PNI.

The liver was the most common site of recurrence in our population. Cho et al. also reported the liver to be the most common metastatic site in patients with early recurrence.²³ Similarly, a study in Iran also showed the liver to be the most common metastasis site for early recurrence.²⁴

The limitations of this study are related to its retrospective nature. As a single-institution study with a small sample size, our results cannot be generalised to the whole population. Furthermore, follow-up duration was too short to determine overall survival and prognostic analysis. A large, multi-institutional study at a national level is required to assess colon cancer and its outcomes in our population, particularly addressing the disparities across rural and urban populations and family income levels. There is a large unmet need to identify predictive markers of recurrence in middle-eastern populations, as data are most commonly acquired in Caucasian ethnicities and validated in Asian studies, highlighting the need for research in under-represented patients in low- and middle-income countries. Our results emphasized the need to recognize the specificities of populations and their risk factors for relapse, to tailor appropriate follow-up schedules, and ensure that curable relapses are identified and the most effective and cost-effective procedures a redelivered.

Our results also demonstrated clinical implications in our settings. In particular, under-performing surgery in terms of resected nodes indicates the need for optimization. Standard follow-up guidelines need to be followed, especially in patients at high risk for recurrence.

Conclusions

To our knowledge, this is the first institutional report on the identification of significant prognostic factors for early postoperative recurrences in resected colon cancer patients in a rural population of Pakistan. Elderly patients and low-quality surgery were significantly associated with increased risk in our subset of rural patients.

Recommendations

We recommend research implementation in low- and middle income countries to emphasize the value of science and knowledge in these patient populations.

Source of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors have no conflict of interest to declare.

Ethical approval

The study was approved by the Institutional Ethical Committee of BINOR.

Authors contributions

SZK conceived and designed the study, conducted research, provided research materials, and collected and organized the data. IF analysed and interpreted data. SZK wrote the initial and final drafts of the article and provided logistic support. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

Acknowledgments

We thank Dario Trapani, MD (Department of Medical Oncology and Hematology, University of Milan and European Institute of Oncology, IRCCS, Milan—Italy) and Angelica Petrillo, MD (Division of Medical Oncology, Department of Precision Medicine, University of Study of Campania ‘Luigi Vanvitelli’, Naples, Italy) for their editorial assistance and manuscript review.

References

- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA. A Clin J Clin* 2018 Nov; 68(6): 394–424. <https://doi.org/10.3322/caac.21492> [cited 2019 Oct 31], Available from:..
- Siegel R, DeSantis C, Jemal A. Colorectal cancer statistics, 2014. *CA. A Clin J Clin* 2014; 64(2): 104–117.
- Association of type 2 diabetes mellitus and the risk of colorectal cancer: A meta-analysis and systematic review [Internet]. [cited 2020 Mar 3]. Available from: <https://www.wjnet.com/1007-9327/full/v21/i19/6026.htm>.
- Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012 - Ferlay - 2015 - International Journal of Cancer - Wiley Online Library [Internet]. [cited 2020 Mar 3]. Available from: <https://onlinelibrary.wiley.com/doi/full/10.1002/ijc.29210>.
- Guraya SY. The prevalence and evolving risk factors for colorectal cancer in the Arab world. *Biomed Pharmacol J* 2018 Dec 25; 11(4): 1773–1780.
- Khan SZ, Fatima I. Tumour sidedness and clinicopathological features of resected colon cancer in rural population of Northern Pakistan: single institutional analysis. *J Coloproctol* 2019 Jul 1; 39(3): 231–236 [cited 2019 Oct 26]. Available from: <http://www.sciencedirect.com/science/article/pii/S2237936319300395>.
- Mahmood S, Faraz R, Yousaf A. Annual cancer registry report-2016, of the Shaukat Khanum memorial cancer hospital & research center, Pakistan. 21 - Google Search [Internet]. [cited 2019 Oct 26]. Available from: https://www.google.com/search?safe=active&rlz=1C1CHBD_enPK775PK775&q=Mahmood+S,+Faraz+R,+Yousaf+A.+Annual+Cancer+Registry+Report-2016,+of+the+Shaukat+Khanum+Memorial+Cancer+Hospital+%26+Research+Center,+Pakistan.+21&spell=1&sa=X&ved=0ahUKewjUq53837nlAhUIAWMBHbvDCO0QBQgrKAA&biw=1366&bih=625.
- Haggar FA, Boushey RP. Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. *Clin Colon Rectal Surg* 2009 Nov; 22(4): 191–197 [cited 2019 Oct 26]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2796096/>.
- Tsai H-L, Chu K-S, Huang Y-H, Su Y-C, Wu J-Y, Kuo C-H, et al. Predictive factors of early relapse in UICC stage I-III colorectal cancer patients after curative resection. *J Surg Oncol* 2009 Dec 15; 100(8): 736–743.
- Tsikitis VL, Larson DW, Huebner M, Lohse CM, Thompson PA. Predictors of recurrence free survival for patients with stage II and III colon cancer. *BMC Canc* 2014 May 16; 14: 336.
- Ryuk JP, Choi G-S, Park JS, Kim HJ, Park SY, Yoon GS, et al. Predictive factors and the prognosis of recurrence of colorectal cancer within 2 years after curative resection. *Ann Surg Treat Res* 2014 Mar; 86(3): 143–151.
- Longo WE, Johnson FE. The preoperative assessment and postoperative surveillance of patients with colon and rectal cancer. *Surg Clin* 2002 Oct; 82(5): 1091–1108.
- Maeda H, Kashiwabara K, Aoyama T, Oba K, Honda M, Mayanagi S, et al. Hazard rate of tumor recurrence over time in patients with colon cancer: implications for postoperative surveillance from three Japanese Foundation for Multidisciplinary Treatment of Cancer (JFMC) clinical trials. *J Canc* 2017; 8(19): 4057–4064 [cited 2019 Oct 26]. Available from: <http://www.jcancer.org/v08p4057.htm>.
- Böckelman C, Engelmann BE, Kaprio T, Hansen TF, Glimelius B. Risk of recurrence in patients with colon cancer stage II and III: a systematic review and meta-analysis of recent literature. *Acta Oncol* 2015 Jan; 54(1): 5–16.
- Elferink MaG, Visser O, Wiggers T, Otter R, Tollenaar RaEM, Langendijk JA, et al. Prognostic factors for locoregional recurrences in colon cancer. *Ann Surg Oncol* 2012 Jul; 19(7): 2203–2211.
- Osterman E, Glimelius B. Recurrence risk after up-to-date colon cancer staging, surgery, and pathology: analysis of the entire Swedish population. *Dis Colon Rectum* 2018; 61(9): 1016–1025.
- Steele SR, Park GE, Johnson EK, Martin MJ, Stojadinovic A, Maykel JA, et al. **The impact of age on colorectal cancer incidence, treatment, and outcomes in an equal-access health care system: diseases of the colon & rectum**, vol. 57; 2014 Mar. pp. 303–310 [cited 2019 Oct 26]. Available from: <http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00003453-201403000-00004>.
- Bouvier A-M, Launoy G, Bouvier V, Rollot F, Manfredi S, Faivre J, et al. Incidence and patterns of late recurrences in colon cancer patients. *Int J Canc* 2015; 137(9): 2133–2138 [cited 2019 Oct 26]. Available from: <https://onlinelibrary.wiley.com/doi/abs/10.1002/ijc.29578>.
- Berger AC, Sigurdson ER, LeVoyer T, Hanlon A, Mayer RJ, Macdonald JS, et al. Colon cancer survival is associated with decreasing ratio of metastatic to examined lymph nodes. *J Clin Oncol* 2005 Dec 1; 23(34): 8706–8712.
- Sakin A, Arici S, Secmeler S, Can O, Geredeli C, Yasar N, et al. Prognostic significance of primary tumor localization in stage II and III colon cancer. *World J Gastrointest Oncol* 2018 Nov 15; 10(11): 410–420.
- Fortea-Sanchis C, Martínez-Ramos D, Escrig-Sos J. CUSUM charts in the quality control of colon cancer lymph node analysis: a population-registry study. *World J Surg Oncol* 2018 Nov 30; 16(1): 230.
- Hatano S, Ishida H, Ishibashi K, Kumamoto K, Haga N, Miura I. Identification of risk factors for recurrence in high-risk stage II colon cancer. *Int Surg* 2013 Jun; 98(2): 114–121.
- Cho YB, Chun H-K, Yun HR, Lee WS, Yun SH, Lee WY. Clinical and pathologic evaluation of patients with recurrence

- of colorectal cancer five or more years after curative resection. *Dis Colon Rectum* 2007 Aug; 50(8): 1204–1210.
24. Aghili M, Izadi S, Madani H, Mortazavi H. Clinical and pathological evaluation of patients with early and late recurrence of colorectal cancer. *Asia Pac J Clin Oncol* 2010 Mar; 6(1): 35–41.

How to cite this article: Khan SZ, Fatima I. Early post-operative recurrences for colon cancer: Results from a Pakistani rural cohort. *J Taibah Univ Med Sc* 2020;15(3):232–237.